R/ concluded

143. The ATIII of claim 142, wherein the ATIII is in a pharmaceutically acceptable formulation.

II. REMARKS

Claims 1-15 are pending in the application. Claims 16-49 were canceled without prejudice in a preliminary amendment filed on December 11, 2001 with the present application. Claims 1-15 are canceled without prejudice herein. New claims 50-143 have been added. Applicants respectfully request allowance of the claims as amended.

Applicants greatly appreciate the granting of the Interview conducted on October 25, 2001, in the parent application, U.S.S.N. 09/305,588 filed on May 5, 1999. Applicants found the Interview very helpful and enjoyed meeting with Examiner Schnizer and Supervisor Low.

Applicants have filed this continuation application to enter claims that reflect the language discussed during the interview and have tried to incorporate the comments as discussed in the interview. There are four groupings of claims in present claims 50-143. Claims 50-67 correspond to claims 50-67 of the parent application, which had been added during prosecution in the parent application, with the additions discussed below, including the addition of a thrombin inhibitory functional requirement, as discussed in the Interview of October 25, 2001. Claims 75-89 are analogous to claims 50-64 except that the claims require a factor Xa inhibitory functional limitation (support for this can be found at least in Table 3). Claims 98-112 are analogous to claims 50-64 except that the thrombin inhibitory functional requirement language is different (support for this can be found at least in Table 3). Claims 121-135 are analogous to claims 75-89 except the factor Xa inhibitory functional requirement

language is different (support for this can be found at least in Table 3). Relative to the language of the claims at the time of the interview on October 25, 2001, claims 50-53, 56, 60, 63-67 have been changed as well, and the corresponding claims in each claim set 75-89, 98-112, and 121-135 reflect these changes as well.

New claims 68 and 69 claim specific embodiments of the compositions and support for these new claims can be found at least in Table 3, on page 57 of the specification which sets forth the specific embodiments claimed. New claims 71 and 73 correspond to claims 3 and 4, but have been amended merely to reflect their new dependency on claim 50. Claims 70, 72, and 74 are dependent claims, incorporating the "pharmaceutically acceptable formulation" language suggested by the Examiner. Claims 90-97, 113-120, and 136-143 correspond to claims 67-74, and correspond to each of the claim sets discussed above, claims 75-89, 98-112, and 121-135.

Claims 1-15 were canceled herein to facilitate prosecution. These claims were canceled without prejudice and Applicants retain the right to prosecute these claims or similar claims in a related application. Claims 50-67 and claims 68-143 clearly indicate that the allowable subject matter includes ATIIIs that are not limited to a specific sequence but include specific mutants surrounding the scissile cleavage site, given the extensive amount that is known about the structure and function of ATIII.

The following discussions for claims in the set of claims 50-74 apply where appropriate to the corresponding claims in the other claim sets discussed herein.

Relative to the language of claims 51 and 52 at the time of the interview on October

25, 2001, claims 51 and 52 now refer to "modifications" instead of "amino acids" to clarify the claims. This does not narrow the scope of claims 51 and 52. Furthermore, this was not done for reasons of patentability, as the claims were particularly defined because one of skill in the art would understand that the additional "amino acids" were modifications to the wild type protein.

Relative to the language of claims 50, 53, 56, 60, and 63-67 at the time of the interview on October 25, 2001, claims 50, 53, 56, 60, and 63-67 now refer to "antithrombin III" rather than "ATIII". This does not narrow the scope of claims 50, 53, 56, 60, and 63-67. Furthermore, this was not done for reasons of patentability, as the claims were particularly defined because one of skill in the art would understand what "ATIII" meant by reference to the claims and specification.

Relative to the language of claims 50, 53, 56, 60, 63, 64, and 67 at the time of the interview on October 25, 2001, claims 50, 53, 56, 60, 63, 64, and 67 now include the phrase "wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^3." Likewise corresponding claims in set 75-97, have the requirement "wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^3," and claims in set 98-120 have the requirement, "wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity," and claims 121-143 have the requirement, "wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity," Support for this can be found at least in Table 3, where various antithrombin activities are described including variant 13A which has a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$

^{1} x 10^{3} and variant Bb.C which has a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^{3}. Furthermore, the variants are compared to plasma ATIII which provides support for the claims drawn to a percent activity of plasma ATIII. This does not narrow the scope of the claims as the previously claimed subject matter was drawn to antithrombin IIIs that retain activity as this is the activity that the variants at the defined positions possess. Nor was this done for reasons of patentability, but rather was done for reasons of clarification that any variants of ATIII must retain that activity.

Applicants have also amended the specification herein by deleting the paragraph starting at page 5, line 22. Applicants respectfully request that the PTO reconsider the United States Patent No. 5,420,252 in light of the new claims and this Amendment to the specification.

A. Rejection in Parent Application Under 35 U.S.C. § 112, ¶2

The Office Action in the parent application, U.S.S.N. 09/305,588 filed on May 5, 1999, dated June 12, 2001, rejected claims 1-13 under 35 U.S.C. § 112, ¶ 2, for allegedly being indefinite. Although the claims have been canceled without prejudice, which obviates this rejection, it was agreed at the Interview of October 25, 2001, that the allowable claim scope would include functional variants of ATIII that incorporated the specific variants at the scissle cleavage bond discussed in the application. As suggested by Supervisor Low, the following correlation is made. Positions 388, 389, 390, 391, 392, and 393 referred to in claims 1-13 refer to the relative positions P6, P5, P4, P3, P2, and P1 respectively.

This rejection would be respectfully traversed.

The Office Action in the parent application, U.S.S.N. 09/305,588 filed on May 5, 1999, dated June 12, 2001 also rejected claims 50-67 under 35 U.S.C. § 112, ¶ 2, for allegedly being indefinite. Claims 50, 53, 56, 60, 63, 64, and 67 now include the phrase "wherein the ATIII retains a thrombin inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^3." Likewise corresponding claims in set 75-97, have the requirement "wherein the ATIII retains a factor Xa inhibitory activity defined by a k_{app} of $0.2M^{-1}sec^{-1}$ x 10^3," and claims in set 98-120 have the requirement, "wherein the ATIII retains a thrombin inhibitory activity which is at least about two percent of plasma ATIII thrombin inhibitory activity," and claims 121-143 have the requirement, "wherein the ATIII retains a factor Xa inhibitory activity which is at least about 12.5 percent of plasma ATIII factor Xa inhibitory activity," as discussed in the Interview of October 25, 2001. It was agreed that the "at least" language was not a problem because of the extensive information known about ATIII structure and that functional variants of ATIII that incorporated the specific variants in the region of the scissle cleavage bond discussed in the application were enabled with functional language added.

This rejection would be respectfully traversed.

Rejection in parent application under 35 U.S.C. § 112, ¶1

The Office Action in the parent application, U.S.S.N. 09/305,588 filed on May 5, 1999, dated June 12, 2001 rejected claims 1-13 under 35 U.S.C. § 112, ¶ 1, for allegedly being based on a disclosure that was non-enabling. Although the claims have been canceled without prejudice, which obviates this rejection, it was agreed at the Interview of October 25, 2001, that the allowable claim scope would include functional variants of ATIII that incorporated the specific variants in the region of the scissle cleavage bond discussed in the application.

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Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of the application to issue.

Respectfully submitted,

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CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this correspondence is being transmitted via Facsimile No. 703-308-4242 addressed to: Attn: Examiner Holly Schnizer, Group Art Unit 1653, U.S. Patent and Trademark Office, on the date shown below.

David E. Huizenga — October 11, 2002 (Date)